

In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) A method for identifying ~~[[an]]~~ a stabilized aptamer that binds to a target molecule, wherein the aptamer comprises at least one 2'-OH guanosine, at least one 2'-OMe guanosine, and at least one of 2'-OMe adenosine, 2'-OMe guanosine, 2'-OMe cytidine or 2'-OMe uridine, including at least one 2'-OMe guanosine, and 2'-OH guanosine (r/mGmH), comprising the steps:

- a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), including at least one 2'-OMe GTP, (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, wherein the concentration of magnesium ions is about 3 to 5 times greater than the concentration of manganese ions, and (vi) one or more double-stranded oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate 2'-OMe NTPs as compared to the ability of the corresponding unmodified RNA polymerase to incorporate 2'-OMe NTPs;
- b) preparing a candidate mixture of stabilized single-stranded nucleic acids by transcribing the one or more oligonucleotide transcription templates under conditions whereby the modified RNA polymerase incorporates the 2'-OMe NTPs, including at least one 2'-OMe GTP, into the stabilized nucleic acids of the candidate mixture, wherein the stabilized single-stranded nucleic acids have a length in the range of 30-50 nucleotides;
- c) contacting the candidate mixture with the target molecule;
- d) partitioning the stabilized nucleic acids having an increased affinity to the target molecule relative to the nucleic acids from the remainder of the candidate mixture; and
- e) amplifying the increased affinity stabilized nucleic acids, in vitro, using the

transcription reaction mixture of step a) to generate a ligand-enriched mixture of nucleic acids, whereby stabilized aptamers comprising at least one 2'-OMe GTP are identified.

2 - 4. (cancelled)

5. (Previously Presented) The method of claim 1, wherein the modified RNA polymerase is a modified T7 RNA polymerase.

6. (Previously Presented) The method of claim 5, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).

7. (Previously Presented) The method of claim 5, wherein the modified T7 RNA polymerase comprises a mutation at position 784 from a histidine residue to an alanine residue (H784A).

8. (Previously Presented) The method of claim 5, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).

9. (Previously Presented) The method of claim 1, wherein the double-stranded oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the template.

10. (Original) The method of claim 9, wherein the leader sequence comprises an all-purine leader sequence.

11. (Previously Presented) The method of claim 10, wherein the all-purine leader sequence

has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

12. (Previously Presented) The method of claim 1, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

13. (Cancelled)

14. (Previously Presented) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM and the concentration of manganese ions is about 1.5 mM.

15. (Previously Presented) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM and the concentration of manganese ions is about 2.0 mM.

16. (Previously Presented) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions is about 9.6 mM and the concentration of manganese ions is about 2.9 mM.

17. (Currently Amended) The method of claim 1, wherein the transcription reaction mixture further comprises ~~a substituted guanosine or guanosine~~ GMP.

18. (Cancelled)

19. (Previously Presented) The method of claim 1, wherein the transcription reaction mixture further comprises polyalkylene glycol.

20. (Previously Presented) The method of claim 19, wherein the polyalkylene glycol is polyethylene glycol.

21 - 76. (Cancelled)

77. (Previously Presented) The method of claim 1, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

78. (Previously Presented) The method of claim 1, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

79. (Previously Presented) The method of claim 6 or claim 7, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

80. (Cancelled)

81. (Currently Amended) The method of ~~claim 80~~ claim 130, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the template.

82. (Previously Presented) The method of claim 81, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

83. (Previously Presented) The method of claim 81, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

84. (Previously Presented) The method of claim 83, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

85. (Previously Presented) The method of claim 84, wherein the transcription reaction mixture further comprises polyethylene glycol.

86-87. (Cancelled)

88. (Previously Presented) The method of claim 8 or 101, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

89. (Cancelled)

90. (Currently Amended) The method of ~~claim 89~~ claim 131, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the template.

91. (Previously Presented) The method of claim 90, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

92. (Previously Presented) The method of claim 91, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

93. (Previously Presented) The method of claim 92, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

94. (Previously Presented) The method of claim 93, wherein the transcription reaction mixture further comprises polyethylene glycol.

95 – 100. (Cancelled)

101. (Currently Amended) A method for identifying ~~[[an]]~~ a stabilized aptamer that binds to a target molecule, wherein the aptamer comprises at least one 2'-OH guanosine, at least one 2'-OMe guanosine, and at least one of 2'-OMe adenosine, 2'-OMe guanosine, 2'-OMe cytidine or 2'-OMe uridine, including at least one 2'-OMe guanosine, and 2'-OH guanosine (r/mGmH) comprising the steps:

- a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), including at least one 2'-OMe GTP, (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, wherein the concentration of magnesium ions is about 3 to 5 times greater than the concentration of manganese ions, and (vi) one or more oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate 2'-OMe NTPs as compared to the ability of the corresponding unmodified RNA polymerase to incorporate 2'-OMe NTPs;
- b) preparing a candidate mixture of stabilized single-stranded nucleic acids by transcribing the one or more oligonucleotide transcription templates under conditions whereby the modified RNA polymerase incorporates the 2'-OMe NTPs, including at least one 2'-OMe GTP, into the stabilized nucleic acids of the candidate mixture, wherein the stabilized single-stranded nucleic acids have a length in the range of 30-50 nucleotides;
- c) contacting the candidate mixture with the target molecule;
- d) partitioning the stabilized nucleic acids having an increased affinity to the target molecule relative to the nucleic acids from the remainder of the candidate

mixture; and

- e) amplifying the increased affinity stabilized nucleic acids, in vitro, using the transcription reaction mixture of step a) to generate a ligand-enriched mixture of nucleic acids, whereby stabilized aptamers comprising at least one 2'-OMe GTP are identified.

102. (Currently Amended) A method for transcribing ~~[[an]]~~ a stabilized oligonucleotide wherein the oligonucleotide comprises at least one 2'-OH guanosine, at least one 2-OMe guanosine, and at least one of 2'-OMe adenosine, 2'-OMe guanosine, 2'-OMe cytidine or 2'-OMe uridine, including at least one 2'-OMe guanosine, and 2'-OH guanosine (r/mGmH) comprising the steps:

- a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), including at least one 2'-OMe GTP, (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, wherein the concentration of magnesium ions is about 3 to 5 times greater than the concentration of manganese ions, and (vi) one or more double-stranded oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate 2'-OMe NTPs as compared to the ability of the corresponding unmodified RNA polymerase to incorporate 2'-OMe NTPs; and
- b) transcribing the one or more oligonucleotide transcription templates under conditions to generate a stabilized transcribed oligonucleotide, whereby the modified RNA polymerase incorporates the 2'-OMe NTPs, including at least one 2'-OMe GTP, into the stabilized transcribed oligonucleotide, and wherein the stabilized transcribed oligonucleotide has a length in the range of 30-50 nucleotides.

103. (Previously Presented) The method of claim 102 or claim 182, wherein the modified

RNA polymerase is a modified T7 RNA polymerase.

104. (Previously Presented) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).

105. (Previously Presented) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 784 from a histidine residue to an alanine residue (H784A).

106. (Previously Presented) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).

107. (Previously Presented) The method of claim 102 or claim 182, wherein the oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the template.

108. (Previously Presented) The method of claim 107, wherein the leader sequence comprises an all-purine leader sequence.

109. (Previously Presented) The method of claim 108, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

110. (Currently Amended) The method of claim 102 or claim 182, wherein the transcription reaction mixture further comprises ~~a substituted guanosine or guanosine~~ GMP.

111. (Cancelled)

112. (Previously Presented) The method of claim 102 or claim 182, wherein the transcription reaction mixture further comprises a polyalkylene glycol.

113. (Previously Presented) The method of claim 112, wherein the polyalkylene glycol is polyethylene glycol.

114. (Previously Presented) The method of claim 102 or claim 182, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

115. (Cancelled)

116. (Previously Presented) The method of claim 102 or claim 182, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM and the concentration of manganese ions is about 1.5 mM.

117. (Previously Presented) The method of claim 102 or claim 182, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM and the concentration of manganese ions is about 2.0 mM.

118. (Previously Presented) The method of claim 102 or claim 182, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions is about 9.6 mM and the concentration of manganese ions is about 2.9 mM.

119. (Previously Presented) The method of claim 102 or claim 182, wherein the 2'-modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

120. (Previously Presented) The method of any one of claims 104, 105 or 106, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

121. (Cancelled)

122. (Currently Amended) The method of ~~claim 121~~ claim 132, wherein the oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the template.

123. (Previously Presented) The method of claim 122, wherein the leader sequence comprises an all-purine leader sequence.

124. (Previously Presented) The method of claim 123, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

125. (Previously Presented) The method of claim 123, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

126. (Previously Presented) The method of claim 125, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

127. (Previously Presented) The method of claim 126, wherein the transcription reaction mixture further comprises polyethylene glycol.

128-129. (Cancelled)

130. (Currently Amended) The method of claim 79, wherein the transcription reaction mixture further comprises ~~a substituted guanosine or guanosine~~ GMP.

131. (Currently Amended) The method of claim 88, wherein the transcription reaction mixture further comprises ~~a substituted guanosine or guanosine~~ GMP.

132. (Currently Amended) The method of claim 120, wherein the transcription reaction mixture further comprises ~~a substituted guanosine or guanosine~~ GMP.

133. (Previously Presented) The method of claim 1, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

134. (Previously Presented) The method of claim 101, wherein the modified RNA polymerase is a modified T7 RNA polymerase.

135. (Previously Presented) The method of claim 134, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).

136. (Previously Presented) The method of claim 135, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

137. (Currently Amended) The method of claim 136, wherein the transcription reaction mixture further comprises ~~a substituted guanosine or guanosine~~ GMP.

138. (Cancelled)

139. (Currently Amended) The method of ~~claim 138~~ claim 137, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the template.

140. (Previously Presented) The method of claim 139, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

141. (Previously Presented) The method of claim 139, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

142. (Previously Presented) The method of claim 141, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

143. (Previously Presented) The method of claim 142, wherein the transcription reaction mixture further comprises polyethylene glycol.

144. (Previously Presented) The method of claim 143, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

145. (Previously Presented) The method of claim 144, wherein the oligonucleotide transcription template is double-stranded.

146. (Previously Presented) The method of claim 134, wherein the modified T7 RNA polymerase comprises a mutation at position 784 from a histidine residue to an alanine residue (H784A).

147. (Previously Presented) The method of claim 146, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

148. (Currently Amended) The method of claim 147, wherein the transcription reaction

mixture further comprises a ~~substituted guanosine or guanosine~~ GMP.

149. (Cancelled)

150. (Currently Amended) The method of ~~claim 149~~ claim 148, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the template.

151. (Previously Presented) The method of claim 150, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

152. (Previously Presented) The method of claim 150, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

153. (Previously Presented) The method of claim 152, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

154. (Previously Presented) The method of claim 153, wherein the transcription reaction mixture further comprises polyethylene glycol.

155. (Previously Presented) The method of claim 154, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

156. (Previously Presented) The method of claim 155, wherein the oligonucleotide transcription template is double-stranded.

157. (Previously Presented) The method of claim 134, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).

158. (Previously Presented) The method of claim 157, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

159. (Currently Amended) The method of claim 158, wherein the transcription reaction mixture further comprises ~~a substituted guanosine or guanosine~~ GMP.

160. (Cancelled)

161. (Currently Amended) The method of ~~claim 160~~ claim 159, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the template.

162. (Previously Presented) The method of claim 161, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

163. (Previously Presented) The method of claim 162, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

164. (Previously Presented) The method of claim 163, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

165. (Previously Presented) The method of claim 164, wherein the transcription reaction mixture further comprises polyethylene glycol.

166. (Previously Presented) The method of claim 165, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

167. (Previously Presented) The method of claim 166, wherein the oligonucleotide transcription template is double-stranded.

168. (Previously Presented) The method of claim 101, wherein the oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the template.

169. (Previously Presented) The method of claim 168, wherein the leader sequence comprises an all-purine leader sequence.

170. (Previously Presented) The method of claim 169, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

171. (Previously Presented) The method of claim 101, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM and the concentration of manganese ions is about 1.5 mM.

172. (Previously Presented) The method of claim 101, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM and the concentration of manganese ions is about 2.0 mM.

173. (Previously Presented) The method of claim 101, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions

is about 9.6 mM and the concentration of manganese ions is about 2.9 mM.

174. (Currently Amended) The method of claim 101, wherein the transcription reaction mixture further comprises a ~~substituted guanosine or guanosine~~ GMP.

175. (Cancelled)

176. (Previously Presented) The method of claim 101, wherein the transcription reaction mixture further comprises polyalkylene glycol.

177. (Previously Presented) The method of claim 176, wherein the polyalkylene glycol is polyethylene glycol.

178. (Previously Presented) The method of claim 101, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

179. (Previously Presented) The method of claim 101, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

180. (Previously Presented) The method of claim 101, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

181. (Previously Presented) The method of claim 101, wherein the oligonucleotide transcription template is double-stranded.

182. (Currently Amended) A method for transcribing [[an]] a stabilized oligonucleotide wherein the oligonucleotide comprises at least one 2'-OH guanosine, at least one 2-OMe

guanosine, and at least one of 2'-OMe adenosine, 2'-OMe guanosine, 2'-OMe cytidine or 2'-OMe uridine, including at least one 2'-OMe guanosine, and 2'-OH guanosine (r/mGmH)
comprising the steps:

- a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), including at least one 2'-OMe GTP, (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, wherein the concentration of magnesium ions is about 3 to 5 times greater than the concentration of manganese ions, and (vi) one or more oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate 2'-OMe NTPs as compared to the ability of the corresponding unmodified RNA polymerase to incorporate 2'-OMe NTPs; and
- b) transcribing the one or more oligonucleotide transcription templates under conditions to generate a stabilized transcribed oligonucleotide, whereby the modified RNA polymerase incorporates the 2'-OMe NTPs, including at least one 2'-OMe GTP, into the stabilized transcribed oligonucleotide, and wherein the stabilized transcribed oligonucleotide has a length in the range of 30-50 nucleotides.

183. (Previously Presented) The method of claim 102 or 182, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

184. (Previously Presented) The method of claim 182, wherein the oligonucleotide transcription template is double stranded.

185. (Previously Presented) The method of claim 127, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

186. (Previously Presented) The method of claim 185, wherein the oligonucleotide

transcription template is double stranded.

187. (Previously Presented) The method of claim 85, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

188. (Previously Presented) The method of claim 94, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

189. (Previously Presented) The method of claim 1, wherein the method further comprises the step:

f) repeating steps c), d) and e) wherein the candidate mixture of step c) is the ligand-enriched mixture of nucleic acids from step e).

190. (Previously Presented) The method of claim 101, wherein the method further comprises the step:

f) repeating steps c), d) and e) wherein the candidate mixture of step c) is the ligand-enriched mixture of nucleic acids from step e).

191. - 194. (Cancelled)

195. (New) The method of claim 1 or claim 101, wherein at least 80% of the guanosine triphosphate nucleotides in the stabilized aptamers are 2'-OMe GTP and the remaining guanosine triphosphate nucleotides in the stabilized aptamers are 2'-OH guanosine triphosphate nucleotides.

196. (New) The method of claim 102 or claim 182, wherein at least 80% of the guanosine triphosphate nucleotides in the stabilized transcribed oligonucleotide are 2'-OMe GTP and the remaining guanosine triphosphate nucleotides in the stabilized transcribed oligonucleotide are 2'-OH guanosine triphosphate nucleotides.